REMARKS

Claims 1, 4, 8, 43, 45, 50, 56, and 57 have been amended. Claims 2, 3, 11-42, 46-49, and 51-55 have been cancelled without prejudice or disclaimer. Claims 1, 4-8, 10, 43-45, 50, 56, and 57 are pending in the instant application. Support for the amendments to the claims can be found in the specification at, for example, page 17, lines 9-11. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

1. Objection to the Specification

The Office Action asserts an objection to the specification because of the use of improperly demarcated trademarks.

Applicant has amended the specification as indicated above to identify the trademarks appearing in the instant application by capitalizing each letter of the mark or by using a proper trademark symbol (*i.e.*, ®). Applicant, therefore, respectfully requests that this objection be withdrawn.

2. Objection to claim 50

The Office Action asserts an objection to claim 50 as depending from non-elected claims.

Applicant has amended claim 50 so that it is no longer depends from non-elected claims, and therefore, respectfully request that this objection be withdrawn.

3. Rejection of claims 1-8, 10, 11, 43-45, 50, 56, and 57 under 35 U.S.C. § 101

The Office Action asserts a rejection of claims 1-8, 10, 11, 43-45, 50, 56, and 57 under 35 U.S.C. § 101. The Action states that the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Applicant traverses this rejection.

Applicant contends that the instant application contains an assertion of a specific and substantial utility for the claimed invention that would be credible to one of ordinary skill in the art. The instant application teaches nucleotide sequences encoding amino acid sequences for two isoforms of TGF–β–R polypeptide (Figures 1A-1B and 2A-2B). The instant application also discloses that a search of the Non-Redundant Protein database, using the amino acid sequence of

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300 South Wacker Drive
Chicago, Illinois 60606
(312) 913-0001

isoforms 1 or 2 of human TGF–β–R polypeptide, indicated that these proteins share the greatest degree of similarity with human and murine Growth Differentiation Factor-3 (GDF-3), and most significantly, that the location and spacing pattern of cysteine residues (which play an important role in GDF-3 structure) is conserved between TGF–β–R polypeptide and GDF-3 (page 80, lines 22-26). Based on the knowledge in the art at the time the instant application was filed, Applicant contends that one of ordinary skill in the art would recognize that TGF–β–R polypeptide is a member of the TGF–β family of proteins. Moreover, based on the expression of human TGF–β–R mRNA in adult prostate, testis, and ovary, and fetal liver (page 81, lines 20-21), and the teaching that TGF–β–R polypeptide shares homology with GDF-3, one of ordinary skill in the art would recognize that the claimed molecules could be useful, for example, in regulating cell growth and development in prostate, testis, ovary, or liver.

Applicant contends that because the instant application contains an assertion of a specific and substantial utility for the claimed invention credible to one of ordinary skill in the art, the rejection under 35 U.S.C. § 101 should be withdrawn.

4. Rejections of claims 1-8, 10, 11, 43-45, 50, 56, and 57 under 35 U.S.C. § 112, first paragraph

The Office Action asserts a rejection of claims 1-8, 10, 11, 43-45, 50, 56, and 57 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention. The Action states that because the claimed invention is not supported by a specific and substantial asserted utility or a well-established utility, one skilled in the art would not know how to use the claimed invention.

Applicant has set forth above affirmative evidence that the asserted utility would be credible to one of ordinary skill in the art. Applicant contends that because the instant application contains an assertion of a specific and substantial utility for the claimed invention that one of ordinary skill in the art would find to be credible, this rejection should be withdrawn.

The Office Action also asserts a rejection of claims 1-8, 10, 11, 43-45, 50, 56, and 57 under 35 U.S.C. § 112, first paragraph, because the specification, were it enabling for the nucleotide sequence of SEQ ID NO: 1 or SEQ ID NO: 3, would not reasonably enable variants or fragments of

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300 South Wacker Drive
Chicago, Illinois 60606
(312) 913-0001

these nucleotide sequences. The Action states that because the specification does not define the biological activity of the polypeptides encoded by the nucleotide sequences of SEQ ID NO: 1 and SEQ ID NO: 3, one of ordinary skill in the art would require undue experimentation to make nucleic acid fragments or variants encoding polypeptides possessing this activity.

Applicant respectfully disagrees with the Action's assertion that the specification does not reasonably enable variants or fragments of the nucleotide sequences of SEQ ID NO: 1 or SEQ ID NO: 3. Nevertheless, in an effort to expedite prosecution of the pending claims to allowance, Applicant has cancelled claims 2 and 3. Applicant reserves the right to pursue claims directed to nucleic acid molecules encoding the TGF-β-R polypeptide variants and fragments recited in claims 2 and 3 in a timely filed continuation or divisional application. Applicant contends that, in view of the specification's teachings and knowledge in the art, it would not require undue experimentation for one of ordinary skill in the art to make and use the nucleic acid molecules of claim 1. Withdrawal of this rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claims 1-8, 10, 11, 43-45, 50, 56, and 57 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that the specification discloses two species of the claimed genus of nucleic acid molecules (*i.e.*, the nucleotide sequences of SEQ ID NO: 1 and SEQ ID NO: 3), and therefore, does not disclose sufficient species for the broad genus of variants of these polynucleotides.

Applicant respectfully disagrees with the Action's assertion that the as-filed claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Nevertheless, as described above, Applicant has cancelled claims 2 and 3 in an effort to expedite prosecution of the pending claims to allowance. Applicant reserves the right to pursue claims directed to nucleic acid molecules encoding the TGF-β-R polypeptide variants and fragments recited in claims 2 and 3 in a timely filed continuation or divisional application. Applicant contends that, in view of the specification's explicit teachings, claim 1 does not contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of

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300 South Wacker Drive
Chicago, Illinois 60606
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the claimed invention. Withdrawal of this rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claims 1-8, 10, 11, 43-45, 50, 56, and 57 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention. The Action states that Applicant's referral to the deposit of plasmids in the specification and claims (*i.e.*, the DNA insert in ATCC Deposit Nos. PTA-2665 or PTA-2666) is an insufficient assurance that all of the conditions of 37 C.F.R. §§ 1.801-1.809 have been met, and that a statement by an attorney of record over his or her signature, stating that a deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent is required. The Action further states that the specification must be amended to recite the date of the deposit, the complete name and address of the depository, and the accession number of the deposited cell line.

Pursuant to the Examiner's request, Applicant's representative submits that Applicant deposited cDNA encoding isoforms 1 and 2 of human TGF–β–R polypeptide with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209. The deposits were accepted by the ATCC, an International Depository Authority, under the provisions of the Budapest Treaty, and the deposits were designated as PTA-2665 or PTA-2666. A copy of the ATCC receipt for these deposits, showing the patent deposit designations (Accession Nos. PTA-2665 or PTA-2666) and the date on which the deposits were received by the ATCC (November 10, 2000) is attached. Pursuant to 37 C.F.R. § 1.808(a)(2), the deposit was made under conditions that assure that all restrictions imposed by the depositors on the availability to the public of the deposited material would be irrevocably removed upon the granting of a patent relying on the deposited biological material. In making the deposit, Applicant acknowledges his responsibility, pursuant to 37 C.F.R. § 1.805, to provide a replacement or supplemental deposit if the depository possessing the deposit is unable to furnish samples thereof or is able to furnish samples thereof but the deposit has become contaminated or has lost its capability to function as described in the specification. With regard to the assertion that the date of the deposit, the complete name and address of the depository, and the accession number of the deposited cell line are not referred to in the body of the specification, Applicant respectfully directs the Examiner's attention to page 78, lines 17-20 of the

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300 South Wacker Drive
Chicago, Illinois 60606
(312) 913-0001

specification as-filed, where Applicant discloses that deposits of cDNA encoding isoforms 1 and 2 of human TGF–β–R polypeptide, subcloned into the pGEMTeasy vector, having Accession Nos. PTA-2665 or PTA-2666, were made with the American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209 on November 10, 2000. Applicant contends that all the requirements of 37 C.F.R. §§ 1.801-1.809 have been met. *In re Lundak,* 225 U.S.P.Q. 90 (Fed. Cir. 1985). Withdrawal of this rejection is therefore respectfully solicited.

Applicant respectfully contends that rejections based on 35 U.S.C. § 112, first paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

5. Rejections of claims 1-8, 10, 11, 43-45, 56, and 57 under 35 U.S.C. § 112, second paragraph

The Office Action asserts a rejection of claims 1-8, 10, 11, 43-45, 56, and 57 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. The Action states that these claims encompass molecules identified by hybridization under moderately stringent conditions, but because the specification does not define such conditions and only presents an example of such conditions, one of ordinary skill in the art would not know what conditions, and thus what molecules, the claims encompass.

Applicant has amended claim 1 to encompass molecules identified by hybridization "under hybridization conditions allowing no more than a 21% mismatch between the nucleotide sequences." Applicant contends that the skilled artisan could use the teachings of the specification and knowledge in the art to determine hybridization conditions in which "no more than a 21% mismatch between the nucleotide sequences" was obtained. For example, the specification discloses that when hybridization is performed at 50°C in a buffer containing 0.015 M Na^+, such results can be obtained. Applicant also contends that one of ordinary skill in the art would appreciate that such results can be obtained using higher temperatures and lower Na^+ concentrations, provided that a denaturing agent (such as formamide) is added to the hybridization buffer. *See, e.g.*, Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual* 6.59-6.60 (3rd ed. 2001) (describing an equation for determining the melting temperature of duplex DNA in a hybridization buffer containing formamide), a copy of

McDonnell Boehnen Hulbert & Berghoff
300 South Wacker Drive
Chicago, Illinois 60606
(312) 913-0001

which is enclosed. Applicant contends that amended claim 1 satisfies the requirements of 35 U.S.C. § 112, second paragraph, and therefore, respectfully request withdrawal of this rejection.

6. Rejections of claims 1-8, 10, 11, and 43-45 under 35 U.S.C. § 102

The Office Action next asserts a rejection of claims 1-8, 10, 11, and 43-45 under 35 U.S.C. § 102(e), as being anticipated by International Publication No. WO 01/92305 (Holloway). The Action states that because Holloway discloses a nucleic acid molecule that is 60% identical to the nucleotide sequence of SEQ ID NO: 1, and which shares a local similarity of 96.9%, the nucleic acid molecule disclosed by Holloway would bind to the complement of SEQ ID NO: 1 under conditions of moderate stringency. Applicant traverses this rejection.

As described in section 5 above, claim 1 has been amended to encompass molecules identified by hybridization "under hybridization conditions allowing no more than a 21% mismatch between the nucleotide sequences." Applicant contends that because the nucleotide sequence disclosed by Holloway shares only 60% identity with the nucleotide sequence of SEQ ID NO: 1, the nucleotide sequence disclosed by Holloway would not hybridize to the nucleotide sequence of SEQ ID NO: 1 "under hybridization conditions allowing no more than a 21% mismatch between the nucleotide sequences." As Holloway does not disclose a nucleotide sequence meeting each and every limitation of the claimed invention, this reference cannot anticipate the pending claims. Applicant, therefore, respectfully requests withdrawal of this rejection.

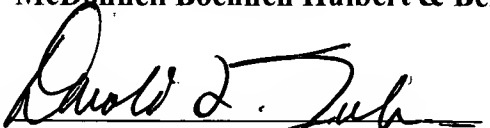
CONCLUSIONS

Applicant respectfully contends that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Andres believes it to be helpful, she is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: December 29, 2003

By: 
Donald L. Zuhn, Ph.D.
Reg. No. 48,710

McDonnell Boehnen Hulbert & Berghoff
300 South Wacker Drive
Chicago, Illinois 60606
(312) 913-0001

ATCC

10801 University Blvd • Manassas, VA 20110-2209 • Telephone: 703-365-2700 • FAX: 703-365-2745

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3 AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Amgen, Inc.
Attn: Dawn Pohl
One Amgen Center Drive, M/S 9-1-C
Thousand Oaks, CA 91320-1799

Deposited on Behalf of: Amgen, Inc.

Identification Reference by Depositor:	**Patent Deposit Designation**
cDNA (human) isloated from human lung tumor: hAMGN-2520-109 (Ref: Docket or Case No.: A-732-P)	PTA-2664
cDNA clone Zhvt-003620 Form I (RDS#200012813): JE3 (Ref: Docket or Case No.: A-696-P)	PTA-2665
cDNA clone Zhvt-003620 Form I (RDS#200009495): JE4 (Ref: Docket or Case No.: A-696-P)	PTA-2666

The deposits were accompanied by: ___ a scientific description _ a proposed taxonomic description indicated above.
The deposits were received November 10, 2000 by this International Depository Authority and have been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested November 15, 2000. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having auth rity to represent ATCC:

Frank Simi ne, Director, Patent D posit ry

Date: November 21, 2000

cc: Scott Bernstein